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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/913,467	12/11/2001	Walter Sebald	086033-000000US	2473

7590 06/17/2005

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EXAMINER

ANDRES, JANET L

ART UNIT	PAPER NUMBER
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1646

DATE MAILED: 06/17/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/913,467

Applicant(s)

SEBALD, WALTER

Examiner

Janet L. Andres

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --
Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 04 April 2005.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-26 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1,2,4-9 and 11-26 is/are rejected.
- 7) ☒ Claim(s) 3,10 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
 - ☐ Certified copies of the priority documents have been received in Application No. _____.
 - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- ☐ Notice of References Cited (PTO-892)
- ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)
Paper No(s)/Mail Date _____.
- ☐ Interview Summary (PTO-413)
Paper No(s)/Mail Date _____.
- ☐ Notice of Informal Patent Application (PTO-152)
- ☐ Other: _____.

RESPONSE TO AMENDMENT

1. Applicant's amendment filed 4 April 2005 is acknowledged. Claims 1-26 are pending and under examination in this office action as they pertain to the elected invention. The text of those sections of Title 35, U.S. Code, not included in this action can be found in a prior office action.

Election/Restrictions

2. Applicant continues to traverse the restriction requirement of 1 June 2004. The restriction requirement was made final in the office action of 29 September 2004 and traversal is no longer considered timely. Applicant's recourse is to petition the director.

Claim Rejections/Objections Withdrawn

3. The objection to claim 20 as containing a typographical error is withdrawn in response to Applicant's amendment.

4. The rejection of claims 16 and 24 under 35 U.S.C. 101 as encompassing non-statutory subject matter is withdrawn in response to Applicant's amendment.

5. The rejection of claims 1, 2, 4-9, and 11-26 under 35 U.S.C. 112, second paragraph, as indefinite is withdrawn in response to Applicant's amendment.

Claim Rejections/Objections Maintained

6. The restriction requirement of 1 June 2004 is maintained for reasons of record above. Therefore the objection to claims 1, 2, 4-9, and 11-26 as encompassing non-elected subject matter is maintained.

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7. The rejection of claims 1, 2, 4-7, 9, and 11-26 under 35 U.S.C. 102(e) as anticipated by U.S. patent application publication 2001/0020086 is maintained for reasons of record in the office action of 29 September 2004.

It is noted that the publication is erroneously cited as "2002/0020068" in the previous office action. However, the citation is correct on the form 892 and Applicant has clearly received the correct reference.

Applicant is correct that the sequence taught is CRKRCN, not CKRKCN. However, as K and R are alternatives in Applicant's sequence this typographical error, while regretted, does not alter the rejection. No reference to Hata was made in the previous office action.

Applicant's argument that CRKRCN (or CKRKCN) has been fully considered but has not been found to be persuasive. As Applicant's SEQ ID NO: 1 is set forth in the entered sequence listing, the first residue could be R. The second residue could be K. The third residue could be R. The fourth residue can be anything that is not K, R, or H and could therefore be C. The fifth residue can be any amino acid that is not K, R, or H and could therefore be N. The sixth residue can be nothing. Thus, the sequence "RKRCN" is encompassed by Applicant's SEQ ID NO: 1. The sequence "CRKRCN" comprises this sequence and thus anticipates Applicant's claims to SEQ ID NO: 1.

8. The rejection of claims 1, 2, 4-7, 9, and 11-26 under 35 U.S.C. 103(a) as unpatentable over the '086 application in view of the '332 patent is maintained for reasons of record in the office action of 29 September 2004.

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Applicant argues that the heparin binding domain of the '086 patent does not meet the structural requirements of claim 1. Applicant further argues that the domains cited in the '332 patent do not meet the requirements of this claim.

Applicant's arguments have been fully considered but have not been found to be persuasive. As stated above, the '086 patent does teach a sequence that meets the structural limitations of claim 1. Similarly, BLI.2 has the sequence IKISGKWKAQKRFLK. The first residue of Applicant's SEQ ID NO: 1 can be K. The second can be R. The third can be nothing. The fourth can be anything but K, R, or H and can thus be F. The fifth can be nothing. The sixth can be anything but K, R, or H, or nothing, and thus can be L. Thus the sequence "KRFL" is encompassed by Applicant's SEQ ID NO: 1. The sequence "IKISGKWKAQKRFLK" comprises this sequence and thus anticipates SEQ ID NO: 1. BLI.3 has the sequence "NVGLKFSISNANIKISGKWKAQKRFLK". It also comprises "KRFL" and therefore anticipates Applicant's SEQ ID NO: 1.

9. The rejection of claim 8 under 35 U.S.C. 103(a) as unpatentable over the '086 patent in view of Linkhart is maintained for reasons of record in the office action of 29 September 2004.

Applicant argues that claim 8 is non-obvious for the reasons discussed for claims 1, 2, 4-7, 9, and 11-26. For the reasons set forth in paragraphs 6 and 7 above the rejection is maintained.

10. The rejection of claims 1, 2, 4-9, and 11-26 under 35 U.S.C. 112, first paragraph, as lacking enablement commensurate in scope with the claims, is maintained for reasons of record in the office action of 29 September 2004.

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Applicant argues that the sequences only require three or four positions, and that there are 17 non-basic possibilities, not 23. Applicant argues again that the prior art does not teach sequences within the limitations of the claims. Applicant argues that claim 1 does not encompass all proteins but only those selected from among members of the DVR family. Applicant argues that there is no explanation as to why the artisan could not predictably identify and use other members of the genus and no objective evidence provided to doubt that a sequence that satisfies the requirements of SEQ ID NO: 1 would bind heparin. Applicant argues that the negatively charged groups of heparin are arranged in triplets and match up with positively charged groups, also arranged in triplets, in the sequence. Applicant argues that introducing such groups into a DVR family member would not introduce significant additional unpredictability, since a wide variety of proteins have heparin binding domains and the capacity of these domains is not dependent on the flanking sequences. Applicant argues that there is nothing difficult in making polypeptide variants and that the artisan would know whether any peptide falls within the scope of claim 1. Applicant argues that simple heparin-binding assays are provided and that a reasonable number of variants having heparin[-binding] activity would be obtained.

Applicant's arguments have been fully considered but have not been found to be persuasive. Applicant is correct that SEQ ID NO: 1 need have only four amino acids, not five, however, this observation merely indicates that the scope of the claims is somewhat broader than was stated by the examiner. Applicant is also correct that there are only 17, not 23, non-basic amino acids. However, this observation fails to significantly narrow the scope of the claims. As set forth above, the sequences cited as prior art are indeed prior art and it is thus noted that in fact members of the claimed genus were not readily recognized by one skilled in the art. While

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Applicant asserts that three positively charged residues are required for heparin binding, Applicant's generic sequence only requires two. Thus, according to Applicant, the essential features of heparin binding are not required by SEQ ID NO: 1. Furthermore, as was stated previously, the '086 and '332 patents teach heparin-binding sequences that are not encompassed by Applicant's sequence. Therefore, Applicant has provided a sequence that does not, by Applicant's assertion, require the features necessary to bind heparin. It requires only four amino acids, of which two can vary among three amino acids and the other two among 17. The remainder of the sequence can be of any length and any composition. Five molecules within the scope of SEQ ID NO: 1 have been shown to bind heparin; other molecules that are not within the scope of the sequence also bind heparin. Thus Applicant's SEQ ID NO: 1 does not describe the essential features of heparin-binding peptides. Thus it would require undue experimentation for the artisan to use members of the genus Applicant has claimed, regardless of the simplicity of making and assaying such members, because the number of encompassed polypeptides is very large and the essential features of heparin binding are not described, and the artisan would not be able to predict which members of this large genus would actually have the desired activity. Furthermore, since the sequences encompassed by the SEQ ID NO: 1 are not limited in size and may be, outside of the requirements discussed above, of almost any composition, it is not predictable that they would have no effect on protein function. That many molecules contain heparin-binding domains is not sufficient guidance to allow the artisan to predict that the sequences so divergent in size and composition could be inserted into molecules with no effect on function; the situation is not analogous.

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Applicant has amended claim 7 to require that the polypeptide be at least 90% homologous. However, the claim still encompasses all “biological activities”. As was stated in the previous office action, no particular activity is required. Thus there is no guidance as to how variants with the same activities could be made and used.

Applicant’s amendment to claim 9 overcomes the aspect of the rejection based on the lack of a cystine knot in the claimed proteins.

With respect to claims 24-26, Applicant’s assertion that the molecules are limited to member of the DVR family is correct. However, according to Applicant’s disclosure, this family includes members such as activins, MIS, nodal, dorsalin, and PTHrP, which do not have known roles in wound healing of any type, and the artisan would thus be unable to use them for this purpose. The therapeutic activity the claimed proteins does not “result from” the improved ability to bind heparin; the specification does not describe conferring such an activity on a protein that does not have said activity. It teaches improvement of activity by increasing heparin binding; see p. 5.

11. The rejection of claims 1, 2, 4-9, and 11-25 under 35 U.S.C. 112, first paragraph, as lacking written description is maintained for reasons of record in the office action of 29 September 2004. Applicant argues that the specification and claims describe structural features commonly possessed by the genus that distinguishes them from others. Applicant argues that the genus is not highly variant, because the sequences have specific structural features and the polypeptides are limited to the “DVR” family.

Applicant’s arguments have been fully considered but have not been found to be persuasive. It is noted, as set forth above, that Applicant did not recognize members of the

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claimed genus. The required structural features are in fact very limited: two amino acids that can be one of three possibilities, and a requirement for two others that cannot be one of these three possibilities. This structural requirement is not sufficient to characterize and identify a genus of heparin-binding sequences. By Applicant's own admission, three positively charged residues are required. Furthermore, as stated above, the cited references teach many heparin-binding factors that do not have even these minimum required characteristics. The claimed genus is in fact highly variant, because the structural requirements are so limited.

The limitation of "DVR" was not discussed in the written description rejection.

12. The objection to claims 3 and 10 as depending from rejected claims is maintained for reasons of record in the previous office action and for the reasons set forth above.

CLAIMS 3 AND 10 ARE OBJECTED TO. CLAIMS 1, 2, 4-9, AND 11-26 ARE REJECTED.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

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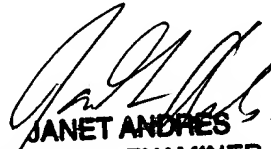
however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Janet L. Andres whose telephone number is 571-272-0867. The examiner can normally be reached on Monday, Tuesday, Thursday, Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa can be reached on 571-272-0829. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Janet L. Andres, Ph.D.
15 June 2005



JANET ANDRES
PRIMARY EXAMINER